Towards an ultra-high resolution macromolecular structural database: analysis of proton acidities and peptide bond deformations by QM calculations, neutron scattering and X-ray crystallography studies.

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Proteins are collections of unique microenvironments instead of aggregates of repeats as its polymeric structure may suggest. Prove of this are the large deviations of pKa values observed for titratable groups present in different protein environments, or the unique properties exhibit by aminoacid side chains in reaction centers. Recent advances in neutron scattering, ultra-high resolution crystallography and the development of refined computational tools allows the exploration of biomolecular microenvironments at an ever increasing level of detail. A recent effort at collecting and cataloging this information has resulted in the HHDB database [1]. Based on the results catalogued on this database and our own analysis of ultra-high resolution structures we have begun the characterization of microenvironments showing the largest deviations from average geometries and occupations in crystal structures. Of particular interest has been the observation of an increasing number of pyramidalized nitrogens in peptide bonds, revealing the presence of H-bond acceptor nitrogens in the backbone. Other interesting result is the direct observation of carbons with labile hydrogens in Histidines. The methods employed to characterize these motifs and the impact of them in our understanding of protein function will be reviewed in this presentation.
[1] http://hhdb01.tokai-sc.jaea.go.jp/HHDB/